

### **REMARKS**

Reconsideration of the objections and rejections set forth in the Office Action dated January 23, 2007 is respectfully requested.

#### **Information Disclosure Statement**

Enclosed is an Information Disclosure Statement which is a re-submission of the IDS which was filed November 1, 2004, along with the requisite fee pursuant to 37 CFR §1.17(p). The attached Forms SB-08 and PTO-892 now contain the serial number of the instant application. It is respectfully requested that the information cited on the attached Forms PTO SB-08 and PTO-892 be expressly considered during the prosecution of the instant application, and that references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

#### **Objections to the Specification**

The Specification was objected to as containing embedded hyperlinks and/or other form of browser-executable code. The Specification has been amended herein to remove the embedded hyperlinks and/or browser-executable code. Withdrawal of this objection is respectfully requested.

The Specification was objected to as allegedly failing to provide proper antecedent basis for the claimed subject matter. The objection with respect to claim 80 is rendered moot by the amendment of that claim. The objection with respect to claim 81 is believed to be overcome by the amendment of that claim to recite "activation of the proteolytic components of complement", support for which is found in the specification at least at page 77 lines 15-16. Accordingly, withdrawal of these objections is respectfully requested.

#### **Status of and Amendments to the Claims**

Claims 73 and 78-81 are amended and new claims 89 and 90 are added herein. Claims 73, 78-81 and 89-90 are pending with entry of this amendment. No new matter has been added by these amendments or the new claims. Support for the claim amendments may be found, for example, at

least on page 7 lines 1-5, page 70 lines 5-27, and page 75 line 5 – page 77 line 18, and original claim 1. Support for new claim 89 may be found, for example, at least on page 75 lines 21-33. Support for new claim 90 may be found, for example, at least at page 75 lines 5 – 10 and page 76 line 28 – page 77 line 4.

Please note that Applicants reserve the right to file subsequent applications claiming any canceled subject matter, and that claim amendments and claim cancellations should not be construed as abandonment of any claimed subject matter.

### **Objections to the Claims**

Claim 73 was objected to for the recitation of the limitation “one or more time” in element (e). This claim has been amended to recite -- one or more times -- as suggested by the Examiner.

Claim 79 was objected to for the recitation of the limitation “selecting selecting the at least”. This objection is rendered moot by the amendment to the claim.

In view of the above, withdrawal of the objections to claims 73 and 79 is respectfully requested.

### **Rejections under 35 USC §112, second paragraph**

Claims 73 and 77-81 were rejected under 35 U.S.C. §112, second paragraph, for indefiniteness. This rejection is respectfully traversed.

Claim 73 (and claims 77-81 due to their dependence from claim 73) was rejected because the source of the nucleic acid selected in step (d) of claim 73 was allegedly unclear. Claim 73 has been amended to clarify that the at least one recombinant immunoglobulin constant region nucleic acid selected in step (d) is selected from the library recited in step (b) by inclusion of the phrase “from the library”. Accordingly, withdrawal of the rejection of claims 73 and 77-81 on this basis is respectfully requested.

Claim 73 (and claims 77-81 due to their dependence from claim 73) was rejected because the “desired property” recited in steps (d) and (e) of claim 73 was allegedly unclear. Claim 73 has been

amended to clarify that the “desired property” recited in step (d) is modified effector function of the Fc region encoded by the at least one recombinant immunoglobulin constant region nucleic acid selected from the library, and that the desired property of step (e) is also modified effector function but at a desired level. New dependent claim 89 further exemplifies step (e). Accordingly, withdrawal of the rejection of claims 73 and 77-81 on this basis is respectfully requested.

Claim 73 (and claims 77-81 due to their dependence from claim 73) was rejected because the claim allegedly did not read back on the preamble. Claim 73 has been amended to clarify that the desired property is modified effector function of the Fc region encoded by the at least one selected recombinant immunoglobulin constant region nucleic acid. Accordingly, withdrawal of the rejection of claims 73 and 77-81 on this basis is respectfully requested.

Claim 73 (and claims 77-81 due to their dependence from claim 73) was rejected as allegedly being incomplete for omitting essential steps. The Office Action asserts that the claim omits process steps wherein the at least one recombinant immunoglobulin constant region nucleic acid is expressed so as to produce a protein product that has an Fc region. Claim 73 has been amended to clarify that the library is expressed and screened for modified effector function and that the at least one recombinant immunoglobulin constant region nucleic acid which encodes a Fc region with the modified effector function is selected from the library. Accordingly, withdrawal of the rejection of claims 73 and 77-81 on this basis is respectfully requested.

Claim 77 (and claim 78 due to its dependence from claim 77) was rejected because the step of selecting the at least one recombinant immunoglobulin constant region nucleic acid *in vitro* was allegedly unclear. Claims 77 and 78 have been amended to conform with amended claim 73 and to clarify that the screening of the library for modified effector function comprises an *in vitro* assay (see, e.g., page 70 lines 5-27 and page 76 line 28 – page 77 line 18 of the specification).

Claim 79 (and claim 80 due to its dependence from claim 79) was rejected because the step of selecting the at least one recombinant immunoglobulin constant region nucleic acid *in vitro* was allegedly unclear. Claims 79 and 80 have been amended to conform with amended claim 73 and to clarify that the screening of the library for modified effector function comprises an *in vivo* assay

(see, e.g., page 70 lines 5-27 and page 76 line 28 – page 77 line 18 of the specification).

Accordingly, withdrawal of the rejection of claims 79 and 80 on this basis is respectfully requested.

Claim 81 was rejected due to allegedly insufficient antecedent basis of the limitation “the desired property”. The Office Action asserts that it is unclear which recitation of a “desired property” in claim 73 this limitation was intended to refer. As noted above, claim 73 has been amended to clarify these terms, and claim 81 has been amended to conform with amended claim 73. Accordingly, withdrawal of the rejection of claims 81 on this basis is respectfully requested.

In view of the above amendments and remarks, it is believed that the claims are clear and definite. Applicants respectfully request that the rejections of claims 73 and 77-81 under 35 U.S.C. §112, second paragraph, be withdrawn.

#### **Rejection under 35 USC §102(b)**

Claims 73, 77 and 79 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Daugherty *et al.* (Nucleic Acids Research 19:2471-2476 (1990), hereinafter “Daugherty”). This rejection is respectfully traversed.

In order for a prior art reference to anticipate an invention, the reference must teach each and every limitation of the claimed invention either expressly or inherently. Daugherty does not teach or suggest each and every limitation of independent claim 73. For example, Daugherty does not teach or suggest recombining a nucleic acid derived from an immunoglobulin heavy chain constant region of an initial antibody with one or more second nucleic acids to produce a library of recombinant immunoglobulin constant region nucleic acids. Instead, Daugherty teaches a method for grafting non-human CDRs (CDR grafting) onto a human framework by overlapping PCR. Furthermore, Daugherty does not teach or suggest expressing such a library of recombinant immunoglobulin constant region nucleic acids, screening the library for modified effector function, and selecting from the library at least one recombinant immunoglobulin constant region nucleic acid which encodes a Fc region which exhibits the modified effector function. Daugherty furthermore does not teach the optional step of repeating the recombining, expressing, screening and selecting steps one or more

times until the Fc region encoded by the selected recombinant immunoglobulin constant region nucleic acid has acquired a desired level of modified effector function. Nor does Daugherty teach screening of the library for modified effector function in an *in vitro* assay, as recited in dependent claim 77, or in an *in vivo* assay, as recited in dependent claim 79. For at least these reasons, Daugherty does not anticipate claim 73 or claims 77 or 79 dependent thereon. Accordingly, withdrawal of the rejection is respectfully requested.

**Rejection under 35 USC §103(a)**

Claims 73 and 77-81 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Daugherty in view of Ward, U.S. Patent 6,277,375 (hereinafter "Ward"). This rejection is respectfully traversed.

To establish a *prima facie* case of obviousness, the combined cited references at the very least must teach or suggest all the claim limitations. The deficiencies of Daugherty have been discussed above. Ward, like Daugherty, does not teach or suggest recombining a nucleic acid derived from an immunoglobulin heavy chain constant region of an initial antibody with one or more second nucleic acids to produce a library of recombinant immunoglobulin constant region nucleic acids. Although Ward describes assays which may be used to assay for modified effector function, these assays are not described in the context of screening a library of recombinant immunoglobulin constant region nucleic acids produced by recombining a nucleic acid derived from an immunoglobulin heavy chain constant region of an initial antibody with one or more second nucleic acids, and selecting from such library at least one recombinant immunoglobulin constant region nucleic acid which encodes a Fc region which exhibits the modified effector function. Ward likewise does not teach the optional step of repeating the recombining, expressing, screening and selecting steps one or more times until the Fc region encoded by the selected recombinant immunoglobulin constant region nucleic acid has acquired a desired level of modified effector function.

Applicants respectfully submit that, at a minimum, the combination of the Daugherty and the Ward references do not teach all of the limitation of claim 73, and thus a *prima facie* case of obviousness cannot be established over claim 73 nor claims 77-81 which depend from claim 73. Accordingly, Applicants respectfully request withdrawal of the §103(a) rejection of pending claims 73 and 77-81 over Daugherty in view of Ward.

### CONCLUSION

This amendment adds two new dependent claims. The total number of claims do not exceed 20. Accordingly, it is believed no fees are due for the added claims. The Commissioner is authorized to charge \$1200 (\$1020 for the Three-Month Extension of Time and \$180 for submission of the Information Disclosure Statement) to Deposit Account No. 50-0990. Please charge any additional fees which may be due, or credit any overpayment, to Deposit Account No. 50-0990.

In view of the amendments and remarks provided above, it is believed that the pending claims are in condition for allowance, and notification to that effect is respectfully requested. Should the Examiner feel that there are any issues outstanding after consideration of this paper, the Examiner is invited to telephone the undersigned at (650) 298-5452.

Respectfully submitted,

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